Rejections based on 35 U.S.C. 112

Claims 1 and 14 have been amended to remove the quantitative limitation of "at least 30 holes in each of two directions" and thus objections based on 35 U.S.C. 112 are believed to have been overcome. Claim 14, additionally, now requires that outmigration of the sample be substantially prevented, as described in the application at p. 8, line 3.

Claim 41 requires loading a specified sample into each through-hole of a subset of an array of through-holes with a density of at least one through-hole per square millimeter. What density is taught in the Specification? At p. 6, line 4, the Specification teaches preferred hole characteristic dimensions of 100-400 μm, while, at lines 6-7, it teaches inter-hole spacing on the order of twice the diameter of the holes. Based on this description, there is at least one hole per linear millimeter, since the hole center spacing is less or equal to 800 μm, while the hole radius is (preferably) 50-200 μm. And one hole per linear millimeter is tantamount to a hole per square millimeter for the rectangular geometry described. Moreover, if the hole size and spacing are *less* than the maximum preferred values presented by way of example in the Specification, then the density would *exceed* one per square millimeter, as claimed.

Moreover, substantially higher densities (10^8 m^{-2}, or 100 per square millimeter) are described explicitly at p. 2, lines 12-13, and these are claimed in claim 4. Thus, claims 41 and 4 are supported in the Specification.

In final regard to the §112 rejections, claims 4-13, 15, and 44 were rejected, it is believed, as infected by the infirmities of base claims 1 and 14, which infirmities have been remedied by amendment herein, and all enablement rejections are believed to have been overcome.

With respect to the prior art advanced in rejection of the claims, the following points are made:

De Macario does not teach through-holes at all.

The claims of the current application are drawn to methods for characterizing samples *using through-holes in a platen.* The through-holes are *open* at each of two substantially parallel planar surfaces. Fig. 1 is a side view, in cross-section, of such a laminated platen. Through-holes traverse platen **10** from one surface **14** to opposing

surface **16** (p. 4, lines 18-19) and must be open at both ends as a matter of definition; holes that are not open on both ends are "blind holes" or, given a range of aspect ratios of depth to width, might be referred to, commonly, as "dishes".

A careful reading of de Marcario shows that de Marcario nowhere contemplates holding samples in a through-hole. All discussion by de Macario of "retaining elements" beginning in the last paragraph of col. 4, continuing in col. 5, teaches that each circular sample-retaining area may be formed as a relatively thin flat **dish**. Again, in col. 7, lines 28-30:

> In this manner, localized reactions may take place within small drops of reaction liquids in the retaining elements, ***that is, on the surfaces of the thin flat dishes***. (emphasis added)

At col. 7, line 43: "Reactive biological substances may be temporarily anchored to a *thin flat dish* . . . ". (emphasis added)

There is *no* reference by de Macario to any retention of samples in holes, but only in dishes. Indeed, there is no appreciation in de Macario of any of the advantages that accrue from employing the methods taught in the present invention, whether advantages of loading, stacking, mixing, dilution, optical interrogation, or optical waveguiding in the through-holes (p. 9, lines 4-5), none of which are taught or suggested, or may even be surmised from any of the teachings of de Macario.

There is no motivation to combine Davis with de Macario.

Davis teaches a method of analyzing *a single* liquid specimen (in fact, instructively, this is the very language of Davis's claim **1**) and a device for supporting such a *single* liquid specimen in order to observe it optically. The specimen support (see description beginning at col. 2, line 51) has one or more disc-like members, each of which has one or more holes that are dipped into a liquid so as to form a film over the holes. There is not a hint of how one might populate different of the Davis specimen support with different samples holes (let alone 'adjacent holes' as required by present claims 1 and 14), or that one might have any reason to. There is thus no motivation to combine Davis with any

reference addressed to the analysis of large numbers of samples, to which the present application is drawn. Thus, Davis fails to overcome the deficiency in de Macario of any teaching of a through-hole.

For this reason, claim 1 (and dependent claims 2-13), claim 14 (and dependent claim 15), and claim 41 are patentable over de Macario and Davis, spearately or in combination.

Rejection based on anticipation by de Macario

Claim 16 is additionally distinguishable over de Macario, not only because de Macario lacks through-holes, but because claim 16, as amended, requires characterizing the contents of multiple through-holes in parallel using an optical configuration as described in the application on pages 8 and 9, with reference to Figs. 6-8. De Macario does not address any optical interrogation at all other than microscopic inspection discussed (with respect to the prior art) at col. 5, beginning at line 40, where there is certainly no apprehension of the issues involved in distinguishing the contents of multiple wells in close proximity. Thus the subject matter of claim 16 , and of claim 17 which depends from it, is neither taught nor suggested by de Marcario, alone or in combination with other references.

Examination and allowance of the claims as amended is requested.

Respectfully submitted,

Samuel J. Petuchowski
Registration No. 31,970
Attorney for Applicant

Bromberg & Sunstein LLP
125 Summer Street
Boston, MA 02110-1618
(617) 443-9292

01118/00174 189526.1

Inventor:	Hunter	Atty Docket:	1118/174
Serial No.:	09/710,082	Art Unit:	1743
Date Filed:	November 10, 2000	Examiner:	A. Soderquist

For: METHOD FOR PERFORMING MICROASSAYS

MARKED UP CLAIMS TO SHOW AMENDMENTS

1. (twice amended) A method for analyzing specified properties of a set of samples, the method comprising:

a. providing a platen having two substantially parallel planar surfaces, an inner layer of hydrophilic material, two outer layers of hydrophobic material coupled to opposite sides of the inner layer, and a two-dimensional array of a plurality of addressable through-holes [having at least 30 holes in each of two directions], the through-holes being disposed substantially perpendicularly to the planar surfaces;

b. loading a first sample into a first set of [at least one of the] through-holes of the two-dimensional array, the first sample being a liquid;

c. retaining the first sample in the first set [at least one] of [the] through-holes by surface tension;

d. adding a second sample into [the at least] a specified through-hole [one of the through-holes], the specified through-hole having at least one adjacent through-hole containing a sample other than the second sample, the specified through-hole further coinciding with one of the first set of at least one of the though-holes [for] thereby permitting a reaction between the first sample and the second sample; and

e. characterizing the reaction in the through-hole in terms of the specified properties.

5. (twice amended) A method according to claim 1 [43], wherein the first sample in liquid form includes at least one of a target in solution and a target in suspension.

6. (twice amended) A method according to claim 1 [43], wherein at least one of a target in solution and a target in suspension includes a biological material.

7. (twice amended) A method according to claim 1 [43], wherein the step of loading a first sample includes drawing the sample from a planar surface by capillary action.

11. (twice amended) A method according to claim 1 [43], further including maintaining a humid atmosphere for preventing evaporation of the first sample.

12. (twice amended) A method according to claim 1 [43], further including coating the liquid sample with a monolayer for preventing evaporation of the first sample.

14. (twice amended) A method for characterizing a plurality of samples of distinct composition, the method comprising:

a. providing a platen having a set of through-holes comprising a two-dimensional array with a density of at least one through-hole per square millimeter[of through-holes having at least 30 holes in each of two directions];

a. loading a specified sample into each through-hole of a first subset of the set of through-holes; [and]

b. loading a second sample into at least one through-hole adjacent to a hole of the first subset of through-holes in such a manner as to substantially prevent capillary outmigration of the second sample; and

d. characterizing a property of the specified sample.

16. (twice amended) A method for analyzing a plurality of samples, the system comprising:

a. loading the samples into a plurality of through-holes disposed in a platen in a two-dimensional array;

b. illuminating [at least one] a set of more than one of the plurality of through-holes with optical radiation; and

c. separately analyzing the optical radiation emanating from each [the at least one] through-hole of the set of more through-holes than one using an optical arrangement including a detector array.